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ning of each regular issue of the PCT Gazette.

(54) Title: ANTIBODIES ANTI-C5 COMPONENT OF THE COMPLEMENT SYSTEM AND THEIR USE

(57) Abstract: The present invention refers to recombinant antibodies of human origin specific for the C5 component of the activated complement and characterised by the ability to inhibit the conversion of the C5 alpha chain to C5a and C5b. Moreover the present invention refers to the nucleotide sequences coding for such antibodies and to the therapeutic use of both polypeptide and nucleotide sequences, in particular for the therapy of diseases involving tissue damage deriving from uncontrolled activation of the complement system.

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## SEQUENCE LISTING

<110> Università degli Studi di Trieste  
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<120> Antibodies anti C5 of the complement and their use

<130> 2728PTWO

<150> MI2002A001527

151> 2002-07-11<160> 35

<170> PatentIn version 3.1

<210> 1

<211> 342

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(342)

<223> Light chain of the TS-A12/22 antibody

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gac atc cgg atg acc cag tct cca gac tcc ctg gct gtg tct ctg ggc 48  
Asp Ile Arg Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly  
1 5 10 15

gag agg gcc acc atc aac tgc aag tcc agc cag agt gtt tta tac agc 96  
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser  
20 25 30

tcc aac aat aag aac tac tta gct tgg tac cag cag aaa cca gga cag 144  
Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln  
35 40 45

cct cct aag ctg ctc att tac tgg gca tct acc cgg gaa tcc ggg gtc 192  
Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val  
50 55 60

cct gac cga ttc agt ggc agc ggg tct ggg aca gat ttc act ctc acc 240  
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr  
65 70 75 80

atc agc agc ctg cag gct gaa gat gtg gca gtt tat tac tgt cag caa 288  
Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln  
85 90 95

tat tat agt act cct cag ctc act ttc ggc gga agg acc aaa gtg gat 336  
Tyr Tyr Ser Thr Pro Gln Leu Thr Phe Gly Gly Arg Thr Lys Val Asp  
100 105 110

atc aaa 342  
Ile Lys

<210> 2

<211> 114

<212> PRT

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20 25 30

Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln  
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val  
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr  
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln  
85 90 95

Tyr Tyr Ser Thr Pro Gln Leu Thr Phe Gly Gly Arg Thr Lys Val Asp  
100 105 110

Ile Lys

&lt;210&gt; 3

&lt;211&gt; 345

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(345)

&lt;223&gt; Heavy chain of the TS-A12/22 antibody

&lt;400&gt; 3

cag gta cag ctg cag cag tca gag gga ggc gtg gtc cag cct ggg agg 48  
Gln Val Gln Leu Gln Gln Ser Glu Gly Gly Val Val Gln Pro Gly Arg  
1 5 10 15

tcc ctg aga ctc tcc tgt gca gcg tct gga ttc acc ttc agt agc tat 96  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30

ggc atg aac tgg gtc cgc cag gct cca ggg aag ggg ctg gag tgg gtt 144  
Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45

tca tac att agt agt agt agt agt acc ata tac tac gca gac tct gtg 192  
Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val  
50 55 60

aag ggc cga ttc acc atc tcc aga gac aat tcc aag aac acg ctg tat 240  
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
 65 70 75 80

ctg caa atg aac agc ctg aga gcc gag gac acg gct gtg tat tac tgt 288  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95

gcg aga ggg cct ggt atg gac gtc tgg gcc caa ggg acc acg gtc acc 336  
 Ala Arg Gly Pro Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr  
 100 105 110

gtc tcc tca 345  
 Val Ser Ser  
 115

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 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
 20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
 35 40 45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val  
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr  
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95

Ala Arg Gly Pro Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr  
 100 105 110

Val Ser Ser  
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<210> 5  
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&lt;221&gt; CDS

&lt;222&gt; (1)..(750)

&lt;223&gt; scFv

&lt;400&gt; 5

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1 5 10 15	
gag agg gcc acc atc aac tgc aag tcc agc cag agt gtt tta tac agc	96
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser	
20 25 30	
tcc aac aat aag aac tac tta gct tgg tac cag cag aaa cca gga cag	144
Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln	
35 40 45	
cct cct aag ctg ctc att tac tgg gca tct acc cgg gaa tcc ggg gtc	192
Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val	
50 55 60	
cct gac cga ttc agt ggc agc ggg tct ggg aca gat ttc act ctc acc	240
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr	
65 70 75 80	
atc agc agc ctg cag gct gaa gat gtg gca gtt tat tac tgt cag caa	288
Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln	
85 90 95	
tat tat agt act cct cag ctc act ttc ggc gga agg acc aaa gtg gat	336
Tyr Tyr Ser Thr Pro Gln Leu Thr Phe Gly Gly Arg Thr Lys Val Asp	
100 105 110	
atc aaa tcc gga ggg tcg acc ata act tcg tat aat gta tac tat acg	384
Ile Lys Ser Gly Gly Ser Thr Ile Thr Ser Tyr Asn Val Tyr Tyr Thr	
115 120 125	
aag tta tcc tcg agc ggt acc cag gta cag ctg cag cag tca gag gga	432
Lys Leu Ser Ser Ser Gly Thr Gln Val Gln Leu Gln Gln Ser Glu Gly	
130 135 140	
ggc gtg gtc cag cct ggg agg tcc ctg aga ctc tcc tgt gca gcg tct	480
Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser	
145 150 155 160	
gga ttc acc ttc agt agc tat ggc atg aac tgg gtc cgc cag gct cca	528
Gly Phe Thr Phe Ser Ser Tyr Gly Met Asn Trp Val Arg Gln Ala Pro	
165 170 175	
ggg aag ggg ctg gag tgg gtt tca tac att agt agt agt agt acc	576
Gly Lys Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Ser Thr	
180 185 190	
ata tac tac gca gac tct gtg aag ggc cga ttc acc atc tcc aga gac	624
Ile Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp	
195 200 205	
aat tcc aag aac acg ctg tat ctg caa atg aac agc ctg aga gcc gag	672
Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu	
210 215 220	

gac acg gct gtg tat tac tgt gcg aga ggg cct ggt atg gac gtc tgg 720  
 Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Pro Gly Met Asp Val Trp  
 225 230 235 240

ggc caa ggg acc acg gtc acc gtc tcc tca 750  
 Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
 245 250

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 <213> Homo sapiens

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Asp Ile Arg Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly  
 1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser  
 20 25 30

Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln  
 35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val  
 50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr  
 65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln  
 85 90 95

Tyr Tyr Ser Thr Pro Gln Leu Thr Phe Gly Gly Arg Thr Lys Val Asp  
 100 105 110

Ile Lys Ser Gly Gly Ser Thr Ile Thr Ser Tyr Asn Val Tyr Tyr Thr  
 115 120 125

Lys Leu Ser Ser Ser Gly Thr Gln Val Gln Leu Gln Gln Ser Glu Gly  
 130 135 140

Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser  
 145 150 155 160

Gly Phe Thr Phe Ser Ser Tyr Gly Met Asn Trp Val Arg Gln Ala Pro  
 165 170 175

Gly Lys Gly Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Ser Thr  
 180 185 190

Ile Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp  
 195 200 205

Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu  
 210 215 220

Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Pro Gly Met Asp Val Trp  
 225 230 235 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
 245 250

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 <212> DNA  
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 <223> CDR1 region of VH

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 Ser Tyr Gly Met Asn  
 1 5

15

<210> 8  
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<400> 8

Ser Tyr Gly Met Asn  
 1 5

<210> 9  
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<220>  
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 <222> (1)..(51)  
 <223> CDR2 region of VH

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tac att agt agt agt agt acc ata tac tac gca gac tct gtg aag  
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 1 5 10 15

48

ggc  
 51

51

<210> 10  
 <211> 17  
 <212> PRT  
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<400> 10

Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys  
 1 5 10 15

Gly

<210> 11  
 <211> 18  
 <212> DNA  
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<220>  
 <221> CDS  
 <222> (1)..(18)  
 <223> CDR3 region of VH

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ggg cct ggt atg gac gtc  
 Gly Pro Gly Met Asp Val  
 1 5

18

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 <212> PRT  
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<400> 12

Gly Pro Gly Met Asp Val  
 1 5

<210> 13  
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 <213> artificial sequence

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 <223> linker

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 <223> linker VL-VH

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 1 5 10 15

48



63

tcc tcg agc ggt acc  
Ser Ser Ser Gly Thr  
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<210> 14  
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<212> PRT  
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<223> linker

<400> 14

Ser Gly Gly Ser Thr Ile Thr Ser Tyr Asn Val Tyr Tyr Thr Lys Leu  
1 5 10 15

Ser Ser Ser Gly Thr  
20

<210> 15  
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<212> PRT  
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<220>  
<221> MISC FEATURE  
<223> Peptide comprising cleavage site of C5 convertase. Corresponding  
to aa 727-744 of mature human protein (P01031).

<400> 15

Lys Asp Met Gln Leu Gly Arg Leu His Met Lys Thr Leu Leu Pro Val  
1 5 10 15

Ser Lys

<210> 16  
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<213> Homo sapiens

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<221> PEPTIDE  
<222> (1)..(20)  
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<400> 16

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1 5 10 15

His Leu Tyr Pro  
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<210> 17  
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<213> Artificial sequence /primer

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33

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94

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41

<210> 22  
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<213> Homo sapiens

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<222> (1)..(33)  
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caggcggcgcg gcgttccttc aactccacct acc

33

<210> 23  
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ccgctactag ttttaccgcg caagcggtcg at

32

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<212> DNA  
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<221> misc\_feature  
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<223> Sequence derived from L27437 GenBank acc. number

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<212> DNA  
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<400> 25

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32

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<211> 36  
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<223> Sequence derived from L27437 GenBank acc. number

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36

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caggcggcgc gcgggctagt cagaaaacca cag

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ccgctactag ttttaccagg aggccgggag atg

33

<210> 29  
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<400> 29

caggcggcgc gccacaaatg ccctacatgc cct

33

<210> 30  
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<222> (1)..(35)  
<223> nucleotide in position 29 is "n"  
Universal oligonucleotide for VL2 amplification.

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<212> DNA  
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<220>  
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<400> 32

caggtgtgca ctcgcagcct gtgctgcary c

31

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<211> 35  
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<220>  
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<400> 33

caggtgtgca ctcgtcctat gwgctgacwc agcca

35

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<400> 34

gacccgcgcg cggagacrgt gaccagggt

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<210> 35  
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<220>  
<221> misc\_feature  
<222> (1)..(29)  
<223> Universal oligonucleotide for JH2 amplification.  
  
<400> 35

gacccgcgcg cagagacggt gaccrktgt

29

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/03/07487

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C07K16/18 C12N15/13 C12N15/63 A61K39/395 C12N5/10  
A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

CHEM ABS Data, SEQUENCE SEARCH, BIOSIS, EPO-Internal, WPI Data, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02 30985 A (TANOX INC) 18 April 2002 (2002-04-18) page 5, line 22 -page 6, line 14 page 13, line 20 -page 16, line 17 page 21, line 9 -page 22, line 2 --- -/--	1-24, 29, 31-36

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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Date of the actual completion of the international search

20 November 2003

Date of mailing of the international search report

12/12/2003

Name and mailing address of the ISA

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Authorized officer

COVONE-VAN HEES, M

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/JP 03/07487

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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International Application No.

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